Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Clinical practice guideline on perinatal hypoxic-ischaemic encephalopathy on newborns.

Bibliographic Source(s)

Guideline Development Group of the Clinical Practice Guideline on Perinatal Hypoxic-Ischaemic[TRUNC]. Clinical practice guidelines on perinatal hypoxic-ischaemic encephalopathy on newborns. Barcelona (Spain): Agency for Health Quality and Assessment of Catalonia (AQuAS); 2015. 263 p. [272 references]

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

NEATS Assessment

National Guideline Clearinghouse (NGC) has assessed this guideline's adherence to standards of trustworthiness, derived from the Institute of Medicine's report Clinical Practice Guidelines We Can Trust.

= Poor = Fair = Good = Very Good = Excellent

Assessment	Standard of Trustworthiness
YES	Disclosure of Guideline Funding Source
	Disclosure and Management of Financial Conflict of Interests
	Guideline Development Group Composition
YES	Multidisciplinary Group
YES	Methodologist Involvement

▮▮▮▮▮	Patient and Public Perspectives
	Use of a Systematic Review of Evidence
▮▮▮▮▯	Search Strategy
▮▮▮▯▯	Study Selection
▮▮▮▮▮	Synthesis of Evidence
	Evidence Foundations for and Rating Strength of Recommendations
▮▮▮▯▯	Grading the Quality or Strength of Evidence
▮▮▮▮▮	Benefits and Harms of Recommendations
▮▮▮▮▮	Evidence Summary Supporting Recommendations
▮▮▮▮▯	Rating the Strength of Recommendations
▮▮▮▮▮	**Specific and Unambiguous Articulation of Recommendations**
▮▮▮▮▯	**External Review**
▮▮▮▮▮	**Updating**

Recommendations

Major Recommendations

Definitions for strength of recommendations (Strong, Weak, Good Clinical Practice [GCP]) are provided at the end of the "Major Recommendations" field.

Risk/Comorbidity Factors

Does the administration of 21% oxygen versus the administration of 100% oxygen during the resuscitation of newborns with a gestational age of greater than or equal to 35 weeks with asphyxia reduce neurological morbidity and mortality?

Recommendations

In newborns with a gestational age of greater than or equal to 35 weeks that require ventilation due to apnea and bradycardia at birth, the guideline development group (GDG) suggests not beginning the administration of 100% O_2. (Weak)

In newborns with a gestational age of greater than or equal to 35 weeks that require ventilation due to apnea and bradycardia at birth, the GDG suggests beginning resuscitation with ambient air or intermediate concentrations of oxygen and suggest that the concentration of O_2 be adjusted according to the patient's clinical response and saturation. (GCP)

Is an Apgar score of 0 at 10 minutes in newborns with a gestational age of greater than or equal to 35 weeks that develop hypoxic-ischaemic encephalopathy (HIE) always related to neurological mortality or

morbidity?

Recommendations

Given that an Apgar score of 0 at 10 minutes is not always related to death or moderate/severe neurological disability, the GDG suggests not using this data by itself to make the decision to limit the therapeutic effort and interrupt resuscitation measures at 10 minutes of life. (Weak)

In newborns with a gestational age of greater than or equal to 35 weeks that show an Apgar score of 0 at 10 minutes of life, the GDG suggests considering a delay in the decision to limit the therapeutic effort. Delaying this decision from 10 minutes of life (Apgar at 10 minutes) to making it in the first hours of life (72 hours) could allow having the results of diagnostic tests that have greater prognostic value and knowing the preferences of the parents. (GCP)

Which of the following factors occurring in newborns with perinatal HIE during the first 72 hours of life (hyperthermia, hypo/hypercapnia, hypo/hyperglycaemia) are associated with greater neurological morbidity and mortality?

Recommendations

In newborns with a gestational age of greater than or equal to 35 weeks with HIE, the GDG recommends avoiding hyperthermia in the first 72 hours of life. (Strong)

In newborns with a gestational age of greater than or equal to 35 weeks with HIE, the GDG recommends avoiding severe hypocapnia (pCO_2 <20 mm Hg) in the first 24 hours of life. (Strong)

In newborns with a gestational age of greater than or equal to 35 weeks with HIE, the GDG suggests avoiding hypercapnia in the first 24 hours of life. (GCP)

In newborns with a gestational age of greater than or equal to 35 weeks with HIE, the GDG recommends avoiding hypoglycaemia in the first 72 hours of life. (Strong)

In newborns with a gestational age of greater than or equal to 35 weeks with HIE, the GDG suggests avoiding hyperglycaemia in the first 72 hours of life. (GCP)

Treatment

In newborns with a gestational age of equal to or greater than 35 weeks with perinatal HIE, does therapeutic hypothermia, in comparison with normothermia, reduce the risk of death or neurological morbidity in the long term?

Recommendations

The GDG recommends the use of hypothermia in newborns with a gestational age of greater than or equal to 35 weeks with perinatal HIE, both moderate and severe, to reduce the risk of death or severe disability in neurodevelopment at 18 to 24 months of age. (Strong)

The GDG recommends the use of hypothermia in newborns with a gestational age of greater than or equal to 35 weeks with perinatal HIE, both moderate and severe, to reduce the risk of death or severe disability in neurodevelopment at 6 to 8 years. (Weak)

The GDG recommends that children with moderate or severe HIE be cared for at hospitals with level III neonatal or paediatric intensive care units with the availability of controlled hypothermia and the capacity to respond to the healthcare complexity of these patients, as well as the availability of proven diagnostic-prognostic tests to establish the severity of the brain damage. (GCP)

In newborns with a gestational age of greater than or equal to 35 weeks with perinatal HIE, does the clinical severity of the encephalopathy determine the effectiveness of treatment with hypothermia?

Recommendation

The GDG recommends the use of hypothermia in newborns with a gestational age of greater than or equal to 35 weeks with perinatal HIE, both moderate and severe, to reduce the risk of death or severe disability in neurodevelopment at 18 to 24 months of age. (Strong)

In newborns with a gestational age of greater than or equal to 35 weeks, is the clinical severity of perinatal HIE during the first 6 hours of life correlated to the risk of death or neurological morbidity in the long term?

Recommendation

In newborns with a gestational age of greater than or equal to 35 weeks with HIE, the GDG recommends, during the first 6 hours of life, that clinical grading systems based on Sarnat's scale be applied to classify the severity of the encephalopathy and to identify candidates for therapeutic hypothermia (patients with moderate or severe encephalopathy). (Strong)

In newborns with a gestational age of greater than or equal to 35 weeks with HIE, has therapeutic hypothermia changed the capacity of the clinical grading of encephalopathy to predict the risk of death or neurological morbidity in the long term?

Recommendation

In newborns with a gestational age of greater than or equal to 35 weeks with HIE, whether or not they are treated with hypothermia, the GDG recommends that the clinical grading of the encephalopathy at 72 hours be used as a tool for predicting the risk of death or severe disability. (Strong)

Are there pharmacological treatments that, initiated in the first hours of life of newborns with a gestational age of greater than or equal to 35 weeks with moderate or severe perinatal HIE, might decrease neurological morbidity and mortality?

Recommendations

In newborns with a gestational age of greater than or equal to 35 weeks with moderate or severe HIE, the GDG suggests not using allopurinol in the first 6 hours of life to reduce death or disability in the short or medium term. (GCP)

In newborns with a gestational age of greater than or equal to 35 weeks with moderate or severe HIE, the GDG suggests not using phenobarbital in the first 6 hours of life to reduce death or disability in the short or medium term. (Weak)

Does the combination of hypothermia with other pharmacological treatments such as topiramate, erythropoietin (EPO), allopurinol or xenon reduce the risk of death or disability at 18 to 24 months in newborns with moderate or severe HIE versus treatment with hypothermia alone in these patients?

Recommendation

In newborns with a gestational age of greater than or equal to 35 weeks with moderate or severe perinatal HIE, the GDG currently suggests not using any pharmacological treatment in conjunction with hypothermia to reduce death or disability. (GCP)

Does the treatment of electrical seizures in newborns with a gestational age of greater than or equal to 35 weeks with HIE, treated or not with therapeutic hypothermia, have an influence on the risk of death or disability at 18 to 24 months?

Recommendations

In newborns with a gestational age of greater than or equal to 35 weeks with HIE and not treated with therapeutic hypothermia and in the presence of electrical seizures, the GDG suggests that anticonvulsant drugs be administered. (Weak)

In newborns with a gestational age of greater than or equal to 35 weeks with significant HIE treated with therapeutic hypothermia, the GDG suggests that anticonvulsant drugs be administered if there are

maintained electrical seizures. (GCP)

Does sedation with opioid derivatives in newborns with HIE (with or without hypothermia) decrease the risk of death or disability at 18 to 24 months?

Recommendation

The GDG suggests routine sedation with opioid derivatives, such as morphine or fentanyl, in newborns with a gestational age of greater than or equal to 35 weeks with HIE treated with hypothermia to decrease the stress and discomfort associated with body cooling and to possibly increase the neuroprotective effect of the hypothermia. (GCP)

Prognostic Studies

In patients with HIE, treated or not with hypothermia, what is the prognostic value of amplitude-integrated electroencephalography (aEEG)?

Recommendations

The GDG suggests the use of aEEG within the first 6 hours of life as a prognostic tool in newborns with HIE. The diagnostic odds ratio (OR) is 30.69 (95% confidence interval [CI]; 10.09 to 93.31) for death/disability in patients not treated with hypothermia and 12.74 (95% CI; 3.24 to 50.16) in patients treated with hypothermia. (Weak)

The GDG recommends the use of aEEG as a prognostic tool of death or severe disability in newborns with HIE as from 6 hours of life. This prognostic value in hours of life is delayed in newborn treated with hypothermia versus those not treated with this therapy: the maximum value was obtained at 24 hours in children not treated with hypothermia (97.5% posttest probability for death/disability; 95% CI, 93.3% to 99.1%) and at 48 hours in children treated with hypothermia (96.9% posttest probability; 95% CI, 81.7 to 99.6%). (Strong)

In patients with HIE, treated or not with hypothermia, what is the prognostic value of brain magnetic resonance imaging (MRI)?

Recommendations

The GDG recommends conducting a cerebral MR study during the first month of life as a prognostic tool in newborns with moderate or severe HIE, whether or not they are treated with therapeutic hypothermia (diagnostic OR of 29.5; 95% CI; 12.12 to 72.25%, and diagnostic OR of 29.80; 95% CI; 17.09 to 51.95%, respectively). (Strong)

In newborns with HIE, whether or not they are treated with therapeutic hypothermia, the GDG recommends conducting a cerebral MRI at between 8 and 30 days to establish the prognosis of death or severe disability. (Strong)

In those patients in which there are prognostic doubts or testing is necessary to orient medical decisions, such as adapting the therapeutic effort, the GDG suggests conducting an early cerebral MRI in the first week of life. The diagnostic OR is 31.05 (95% CI; 10.69 to 90.84) for death/disability in patients not treated with hypothermia and 48.34 (95% CI; 1.85 to 1246.90) in children treated with hypothermia. (Strong)

What is the prognostic value of the biomarkers in blood, urine or cerebral spinal fluid (CSF) to predict death or neurodevelopmental problems in newborns with moderate or severe HIE, treated or not with hypothermia?

Recommendation

In newborns with a gestational age of greater than or equal to 35 weeks with HIE, and who are stable and without refractory coagulopathy, the determination of neuron-specific enolase (NSE) in CSF in the first 72 hours of life should be considered, particularly if additional information is required to establish

the prognosis or make decisions about limiting the therapeutic effort. (Strong)

Follow-up

Do the current data for predicting neurological damage based on both clinical data and/or the pattern of involvement in the neuroimaging MRI (NMRI) allow establishing differentiated and effective programmes of neurodevelopmental follow-up?

Recommendations

The follow-up on newborns with perinatal HIE and the duration thereof should be planned individually according to both biological risk factors (severity of the encephalopathy, type of brain injury) and family and social factors. (GCP)

Children with moderate or severe HIE must be cared for at a hospital centre with access to treatment using hypothermia and to the various prognostic tests indicated in this CPG. (GCP)

Assessments should be scheduled considering the age of appearance of each one of the complications and the specific risk that such complications could appear in each child. (GCP)

Given the diversity and complexity of the problems that appear after being discharged from the hospital, caring for these children requires a multidisciplinary approach. (GCP)

Both children with a high risk of death after being discharged from the hospital and their families require special care targeted at anticipating the complications that lead to death, at optimising care at the end of life and at taking care of family needs related to grief. (GCP)

Definitions

Implications of the Grades of Recommendations in the Grading of Recommendations Assessment, Development and Evaluation (GRADE) System

Implications of a:	Strong Recommendation	Weak Recommendation
Patients	The vast majority of people would agree with the recommended action, and only a small proportion would not.	The majority of people would agree with the recommended action, but a considerable number of people would not.
Clinicians	The majority of patients should receive the recommended intervention.	It recognises that various options will be appropriate for different patients and that the health professional has to help each patient reach a decision that is the most consistent with their values and preferences.
Managers/Planners	The recommendation can be adopted as a health policy in the majority of situations.	Considerable debate is necessary, in addition to participation by stakeholders.

Likewise, "guidelines of good clinical practice" have been formulated, based on the clinical experience of the coordination team regarding important practical aspects that the guideline development group has wanted to emphasise and about which there is no supporting scientific evidence.

Clinical Algorithm(s)

An algorithm titled "Management Algorithm for Newborns at Risk of Perinatal Hypoxic-Ischaemic Encephalopathy" is provided in the original guideline document.

Scope

Disease/Condition(s)

Hypoxic-ischaemic encephalopathy

Note:

The guideline development group understands encephalopathy during the first days of life to be a neurological syndrome that is present as from birth and is characterised by difficulties to initiate or maintain respiration and by alterations in the ability to wake up or remain awake (alert) and alterations in muscle tone and in excitability, with or without convulsions.
The perinatal hypoxic-ischaemic origin of the encephalopathy will be defined by:

The presence of an obstetric background of risk (sentinel event, non-reassuring foetal status or labour dystocia) and/or
An altered perinatal status defined by an Apgar of less than 5 at 5 or 10 minutes and/or an umbilical artery pH or a pH in the first hour of life of the newborn of less than 7.00 and/or a base deficit of greater than 12 mmol/L.

Guideline Category

Diagnosis

Evaluation

Risk Assessment

Treatment

Clinical Specialty

Critical Care

Emergency Medicine

Internal Medicine

Neurology

Obstetrics and Gynecology

Pediatrics

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Emergency Medical Technicians/Paramedics

Health Care Providers

Hospitals

Nurses

Occupational Therapists

Patients

Physical Therapists

Physician Assistants

Physicians

Social Workers

Speech-Language Pathologists

Guideline Objective(s)

- To prepare a clinical practice guideline (CPG) that provides healthcare professionals and the families of these children with a tool, based on scientific evidence, that helps them to make therapeutic, diagnostic, prognostic and follow-up decisions that are tackled in the care of neonates with hypoxic-ishaemic encephalopathy (HIE)
- To establish recommendations for the purpose of supporting, in the entire National Health System, the decisions of healthcare professionals involved with neonates with HIE. These recommendations will affect elements of resuscitation, comorbidity conditions in the first hours, diagnosis, treatment, prognosis and follow-up.
- To evaluate the cost-effectiveness, ethical, cultural and organisational aspects that must be taken into account in the recommendations
- To examine the impact on families and provide useful information for parents (or relatives/caregivers) whose children have HIE in order to offer them the help and support they need, as well as establish actions that facilitate their parental role in this difficult circumstance

Target Population

Newborns with a gestational age of greater than or equal to 35 weeks with perinatal hypoxic-ischaemic encephalopathy

Note: This CPG does not cover:

Either the handling or the consequences of perinatal hypoxic-ischaemic injury in newborns ≤35 weeks of gestation.
Neonatal encephalopathy whose primary origin is of a haemorrhagic, infectious, metabolic or toxic pathology.
Newborns with encephalopathy but with congenital malformations of the central nervous system or severe genetic anomalies.
Newborns with a focal ischaemic injury in the tributary region of a specific vessel (perinatal stroke).
Neonatal encephalopathy due to potential postnatal hypoxic-ischaemic injury in full-term newborns, such as the so-called neonatal collapse.
Organisational aspects or care models that are required to put the recommendations into practice.

Interventions and Practices Considered

1. Resuscitation with ambient air or intermediate concentrations of oxygen
2. Use of Apgar score at 10 minutes
3. Avoidance of hyperthermia, hypercapnia, severe hypocapnia, hypoglycaemia, and hyperglycaemia
4. Hypothermia
5. Provision of care at Level III neonatal or paediatric intensive care units
6. Use of clinical grading systems based on Sarnat's scale
7. Anticonvulsant drugs
8. Routine sedation with opioid derivatives (morphine, Fentanyl)
9. Amplitude-integrated electroencephalography (aEEG)
10. Cerebral magnetic resonance imaging (MRI)
11. Determination of neuron-specific enolase in cerebral spinal fluid
12. Follow-up
13. Multidisciplinary approach

Note: The following were considered but not recommended: 100% O_2, allopurinol, phenobarbital, pharmacological treatments in conjunction with hypothermia (topiramate, erythropoietin [EPO], allopurinol, xenon).

Major Outcomes Considered

- Morbidity
- Mortality

- Cerebral palsy
- Moderate/severe disability
- Epilepsy
- Convulsions
- Survival with normal neurological function
- Adverse effects
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The formulation of clinical questions followed the Patient-Intervention-Comparison-Outcome (PICO) format.

A bibliographical search in: CMA Infobase, DARE (only systematic reviews), National Guideline Clearinghouse, Cochrane, Fisterra, Google, Guidelines International Network, PubMed, CINAHL, Scopus, Tripdatabase, Web of Knowledge Center of Review and Dissemination, Eguidelines, Doc's CISMEf, GuíaSalud, NHR Health Technology Assessment Programme, NHS Evidence, Scottish Intercollegiate Network, UK Health Centre, UpToDate, Web Hospital, Web Rafa Bravo, Clinical Trials, Clinical Trials Register, Current Controlled Trials and NHSEED.

Searches were conducted between February 2012 and April 2012, with alerts that were maintained until January 2013. The language was only an excluding factor at the time when the complete text of observational studies written in Chinese, Japanese and Russian were obtained. In the first phase, a preliminary search of clinical practice guidelines (CPGs) (used as secondary sources of evidence) and of systematic reviews was conducted in the aforementioned databases. In a second phase, an expanded search of original studies (randomized controlled trials [RCTs]) was conducted in PubMed, Cochrane and CINHAL. The search was expanded to observational studies (third phase) when the clinical question was not answered with the documents identified in the previous phases. Searches of qualitative studies (in PubMed, PsycINFO and CINAHL) and of economic evaluations (PubMed and NHSEED) were conducted. Alerts were activated in PubMed until January 2013. The search strategy is presented in Appendix 2 in the original guideline document.

The methodology used to prepare this clinical practice guideline (CPG) is included in the *Methodology Manual for Drafting CPGs in the National Health System (NHS)* (see the "Availability of Companion Documents" field).

Number of Source Documents

Refer to the Methodological Material document (see the "Availability of Companion Documents" field) for a breakdown of the identified studies and included studies for each clinical question.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Classification of the Quality of Evidence in the GRADE System

Quality of the Scientific Evidence	Design of the Study	Decrease the quality if	Increase the quality if
High	RCTs	Limitation in the design: Important (-1) Very important (-2) Inconsistency (-1) Direct evidence: Some (-1) uncertainty Major (-2) uncertainty about whether or not the evidence is direct Inaccurate data (-1) Notification bias: High probability of (-1)	Association: scientific evidence of a strong association (RR>2 or <0.5 based on observation studies without confusion factors) (+1) Scientific evidence of a very strong association (RR>5 or <0.2 based on studies without the possibility of bias) (+2) Dose-response gradient (+1) All the possible confusion factors could have reduced the observed effect (+1)
Moderate			
Low	Observational studies		
Very Low	Other types of design		

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Synthesis and evaluation of the quality of the evidence. The two clinical practice guidelines (CPGs) on perinatal hypoxic-ischaemic encephalopathy that were found were independently evaluated by two components of the development group using the AGREE II (Appraisal of Guidelines Research and Evaluation) instrument. Systematic reviews were evaluated using the broken-down criteria of AMSTAR (A Measurement Tool to Assess Systematic Reviews). For the economic evaluations, the criteria described by López-Bastida et al. were used. The group agreed upon a series of aspects for evaluating the quality of primary studies, which varied depending on whether they were evaluation studies of diagnostic tests or predictive strategies of interventions or of risk factors (see Appendix 2 of the Methodological Material [see the "Availability of Companion Documents" field]).

Final evaluation of the quality of studies and a summary of the evidence for each question, therefore following the Grading of Recommendations Assessment, Development and Evaluation (GRADE).

The methodology used to prepare this clinical practice guideline (CPG) is included in the *Methodology Manual for Drafting CPGs in the National Health System (NHS)* (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Formation of the guideline development group, integrated by professionals: specialists in paediatrics (neonatologists), clinical psychology, nursing and methodology (evidence-based medicine, clinical practice guideline [CPG] drafting, qualitative research and economic evaluation). To incorporate the values and preferences of the parents, relatives and caregivers of newborns with perinatal hypoxic-ischaemic encephalopathy (HIE) when formulating the recommendations of the CPG and to prepare information for parents, relatives and caregivers, a qualitative study was conducted.

The formulation and grading of recommendations was done according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. Controversial recommendations or those with an absence of evidence were resolved by consensus in a meeting attended in person by members of the development group.

The methodology used to prepare this clinical practice guideline (CPG) is included in the *Methodology Manual for Drafting CPGs in the National Health System (NHS)* (see the "Availability of Companion Documents" field).

Rating Scheme for the Strength of the Recommendations

Implications of the Grades of Recommendations in the Grading of Recommendations Assessment, Development and Evaluation (GRADE) System

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Clinicians	The majority of patients should receive the recommended intervention.	It recognises that various options will be appropriate for different patients and that the health professional has to help each patient reach a decision that is the most consistent with their values and preferences.
Managers/Planners	The recommendation can be adopted as a health policy in the majority of situations.	Considerable debate is necessary, in addition to participation by stakeholders.

Likewise, "guidelines of good clinical practice" have been formulated, based on the clinical experience of the coordination team regarding important practical aspects that the guideline development group has wanted to emphasise and about which there is no supporting scientific evidence.

Cost Analysis

The guideline developers reviewed published cost analyses.

Refer to the "Costs and Use of Resources" sections in the original guideline document for additional information.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The expert collaborators reviewed both the questions and the selected studies, the tables of evidence and the recommendations. The outside reviewers participated in the review of the first draft of the guideline. Various scientific societies were contacted (Spanish Society of Neonatology, Spanish Society of Paediatrics, Spanish Society of Obstetrics and Gynaecology, Spanish Society of Neonatal Nursing, Spanish Society of Paediatric Intensive Care, Spanish Society of Paediatric Anaesthesiology, Hipo SEN and Cat), as well as the most relevant experts at the state level who take part in the treatment and care of these patients. Given that there are no associations of parents of children with hypoxic-ischaemic encephalopathy (HIE) established in Spain, none could be contacted.

The methodology used to prepare this CPG is included in the *Methodology Manual for Drafting CPGs in the National Health System (NHS)* (see the "Availability of Companion Documents" field).

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Refer to the "Balance Between Benefits and Risks" sections of the original guideline document for further discussion of potential benefits of individual recommendations.

Potential Harms

Refer to the "Balance Between Benefits and Risks" sections of the original guideline document for further discussion of potential harms of individual recommendations.

Qualifying Statements

Qualifying Statements

This clinical practice guideline (CPG) is an aid for decision making in health care. It is not mandatory, and it is not a substitute for the clinical judgement of healthcare personnel.

Implementation of the Guideline

Description of Implementation Strategy

Strategies for Disseminating and Implementing the Clinical Practice Guideline (CPG)

The plan for disseminating and implementing the CPG on perinatal hypoxic-ischaemic encephalopathy (HIE) in newborns includes the following interventions:

Preparation of a summarised version and a quick guide (algorithms and annotations) in an on-line format.
Promotion of the CPG by health authorities through media for healthcare professionals.
Dissemination of the CPG on at least the official web pages of scientific companies that participate in reviewing the guide and on all others indirectly related to the health of newborns.
Proposal for inclusion of the CPG in databases that compile guidelines at the state and international levels (National Guideline Clearinghouse: http://guideline.gov/).
Distribution of a parents' guide among hospitals that provide therapeutic hypothermia.
Free access to the various versions of this CPG at the following Web pages: Agency for Health Quality and Assessment of Catalonia (AQUAS) (http://aquas.gencat.cat); Fundació Hospital Sant Joan de Déu (www.fsjd.org/es); the journal *Evidencias en Pediatría*; and the Web page of the Department of Health through Canal Salut (http://aquas.gencat.cat/).
Presentation of the results of the CPG in scientific activities (conferences, workshops, meetings) and particularly in professional education courses related to the handling of neonatal patients with HIE.
Distribution of the CPG to professional bodies, health administrations, health centres and professional associations.
Publication of information about the CPG in specialised journals and publications, particularly attempting to have it reviewed in *Anales de pediatría*, the most widely distributed national journal with the greatest weight within the professional scope of paediatrics.

Refer to the original guideline document for additional information on the implementation strategy.

Implementation Tools

Clinical Algorithm

Foreign Language Translations

Mobile Device Resources

Patient Resources

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Safety

Identifying Information and Availability

Bibliographic Source(s)

Guideline Development Group of the Clinical Practice Guideline on Perinatal Hypoxic-Ischaemic[TRUNC]. Clinical practice guidelines on perinatal hypoxic-ischaemic encephalopathy on newborns. Barcelona (Spain): Agency for Health Quality and Assessment of Catalonia (AQuAS); 2015. 263 p. [272 references]

Adaptation

Not applicable: The guideline is not adapted from another source.

Date Released

2015

Guideline Developer(s)

Agency for Health Quality and Assessment of Catalonia - State/Local Government Agency [Non-U.S.]

GuiaSalud - National Government Agency [Non-U.S.]

Ministry of Health (Spain) - National Government Agency [Non-U.S.]

Guideline Developer Comment

Collaborating Societies

Members of these societies or associations have participated in the external review of the clinical practice guideline (CPG):

- Spanish Association of Paediatrics (AEP)
- Spanish Association of Primary Care Paediatrics (AEPap)
- Federation of Associations of Midwives of Spain (FAME)
- Hypothermia Group of Catalonia (HIPOCAT)
- Hypothermia Group of the Spanish Society of Neonatology (HipoSEN)
- Spanish Society of Anaesthesiology, Resuscitation and Pain Therapy (SEDAR)
- Spanish Society of Neonatal Nursing (SEEN). Spanish Society of Neonatology (SENeo)
- Spanish Society of Paediatric Neurology (SENEP)
- Spanish Society of Obstetrics and Gynaecology (SEGO)

Source(s) of Funding

This clinical practice guideline (CPG) has been funded through the agreement signed by the Institute of Health Carlos III (ISCIII), an autonomous body of the Ministry of Economy and Competitiveness, and the Agència de Qualitat i Avaluació Sanitàries de Catalunya, within the framework of developing activities by

the Spanish Network of Agencies for Health Technology Assessment and National Health Service (NHS) benefits, financed by the Ministry of Health, Social Services and Equality.

Guideline Committee

Clinical Practice Guideline on Perinatal Hypoxic-Ischaemic Encephalopathy in Newborns Guideline Development Group

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

All members of the Development Group, as well as those who participated in the expert collaboration and external review, made the declaration of interest below.

Declaration of Interests

Guideline Development Group of the Clinical Practice Guideline (CPG) on Perinatal Hypoxic-Ischaemic Encephalopathy

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Albert Balaguer Santamaría received aid from the pharmaceutical industry in 2010, managed from his service to attend a national conference on paediatrics. In 2011, he received financing from the Instituto Carlos III to work on a research project not related to this CPG.

Nuria Herranz Rubia received professional fees as a speaker for Abbot in 2008 regarding a conference on the Hera project.

Dorotea Blanco Bravo received professional fees as a speaker for Covidien in 2011.

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Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available in English and Spanish from the GuíaSalud Web site.

Availability of Companion Documents

The following are available:

Quick reference guides and summary versions are available in Spanish from the GuíaSalud Web site.

Clinical practice guideline on perinatal hypoxic-ischaemic encephalopathy on newborns. Methodological material. Barcelona (Spain): Agency for Health Quality and Assessment of Catalonia (AQuAS); 2015. 220 p.

Preparation of clinical practice guidelines in the National Health System. Update of the methodological manual. Available in Spanish from the GuíaSalud Web site.

Working Group for CPG Updates. Updating clinical practice guidelines in the National Health System: methodology handbook. Madrid (Spain): National Health System Quality Plan of the Spanish Ministry of Health and Social Policy; Aragon Institute for Health Sciences (IACS); 2009. 67 p. (Clinical Practice Guidelines in the National Health System: IACS; no. 2007/02-01). Available from the GuíaSalud Web site.

The Spanish version of the guideline is also available via a mobile application from the GuiaSalud Web site.

Patient Resources

Patient information can be found in Appendix 1 of the original guideline document. A Spanish version is also available from the GuíaSalud Web site.

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